CLAIMS

1. A nucleic acid molecule encoding a protein having the biological activity of a tumor suppressor selected from the group consisting of:

(a) nucleic acid molecules coding for a polypeptide comprising the amino acid sequence given in SEQ ID NO.2;

(b) nucleic acid molecules comprising the nucleotide sequence given in SEQ ID NO.1;

(c) nucleic acid molecules hybridizing to a nucleic acid molecule as defined in (a) or (b); and

(d) nucleic acid molecules, the nucleotide sequence of which is degenerate as a result of the genetic code to a nucleotide sequence of a nucleic acid molecule as defined in (a), (b) or (c).

2. A method for the identification and cloning of nucleic acid molecules encoding a protein having the biological activity of a tumor suppressor comprising the steps of:

(i) transfecting mammalian cells with

(a) a first vector comprising a scorable reporter gene operatively linked to regulatory elements comprising at least one cAMP responsive element so located relative to said reporter gene to permit cAMP inducible expression thereof; and

(b) pools of expression vectors comprising nucleic acid molecules linked to regulatory elements allowing expression in the mammalian cells;

(ii) cultivating the transfected cells under conditions which permit expression of the nucleic acid molecules present in the vectors;

(iii) identifying those vector pools which lead after transfection to expression of said reporter gene in the mammalian cells;

(iv) optionally subdividing the vector pool(s) identified in step (iii) and repeating step (i) to (iii); and

(v) isolating from the so-identified vector pool(s) the nucleic acid molecule present in the vector(s) and testing its product for tumor suppressor activity.

3. The method of claim 2, wherein in step (ii) a ligand of a receptor which is capable of increasing the level of intracellular cAMP is added to the culture medium.

4. The method of claim 3, wherein the ligand is the peptide PACAP.

a 5. The method of ~~any one of claims 2 to 4~~ claim 2, wherein the mammalian cells are LLC-PK1 cells (ATCC CC101) or Saos-2 cells (ATCC HTB 85).

a 6. The method of ~~any one of claims 2 to 5,~~ claim 2 wherein the cAMP responsive element is derived from a corticotropin releasing hormone gene.

a 7. The method of ~~any one of claims 2 to 6,~~ claim 2 wherein the regulatory elements controlling the reporter gene are derived from MMTV.

a 8. The method of ~~any one of claims 2 to 7,~~ claim 2 wherein the reporter gene codes for a luciferase.

a 9. The method of ~~any one of claims 2 to 8,~~ claim 2 wherein the nucleic acid molecules present in the vectors of the vector pool are cDNAs.

10. The method of claim 9, wherein the cDNA is prepared from RNA obtained from mammalian, bacterial, fungal or plant cells or viruses.

11. A nucleic acid molecule obtainable by a method of ~~any one of claims 2 to 10~~ claim 2 which encodes a protein having tumor suppressor activity.

12. A nucleic acid molecule which hybridizes to a nucleic acid molecule of claim 1 ~~or claim 11~~ and which encodes ~~a~~ said mutated version of a protein ~~as defined in claim 1 and 11~~ which has lost its tumor suppressor activity.

13. The nucleic acid molecule of claim 1, ~~11 or 12~~ which is DNA.

14. The nucleic acid molecule of claim 13 which is cDNA.

15. The nucleic acid molecule of claim 1 or ~~of any one of claims 11 to 14,~~ which is derived from a mammal.

16. The nucleic acid molecule of claim 15, wherein the mammal is human or mouse.

17. The nucleic acid molecule of claim 16, wherein the nucleic acid molecule comprises a nucleotide sequence encoding the amino acid sequence given in SEQ ID NO. 17 or the nucleotide sequence given in SEQ ID NO. 16.

18. A nucleic acid molecule of at least 15 nucleotides in length hybridizing specifically with a nucleic acid molecule of claim 1 or with a nucleic acid molecule of any one of claims 11 to 17 or to a complementary strand thereof.

19. A vector comprising a nucleic acid molecule of claim 1 or of any one of claims 11 to 17.

20. The vector of claim 19, wherein the nucleic acid molecule is operatively linked to regulatory elements permitting expression in prokaryotic and/or eukaryotic host cells.

21. A host cell comprising a vector of claim ~~19 or 20~~.

22. The host cell of claim ~~21~~, which is a bacterial, fungal, plant or animal cell.

23. The host cell of claim ~~22~~, which is a mammalian cell.

24. Method for the production of a polypeptide having the biological activity of a tumor suppressor comprising culturing a host cell of claim ~~22 or 23~~ under conditions allowing the expression of the polypeptide and recovering the produced polypeptide from the culture.

25. A polypeptide encoded by a nucleic acid molecule of claim 1 or of any one of claims 11 to 17 or produced by a method according to claim 24.

26. An antibody specifically recognizing a polypeptide of claim 25.

27. A pharmaceutical composition comprising a nucleic acid molecule of claim 1 or of any one of claims 11 to 17, or a nucleic acid molecule which is complementary to such a nucleic acid molecule, a nucleic acid molecule of claim 18, a vector of claim 19 or 20, a polypeptide of claim 25 and/or an antibody of claim 26, and optionally a pharmaceutically acceptable carrier.

28. A diagnostic composition comprising a nucleic acid molecule of claim 1, or of any one of claims 11 to 17 or a nucleic acid molecule which is complementary to such a nucleic acid molecule, a nucleic acid molecule

of claim 18, a vector of claim 19 or 20, a polypeptide of claim 25 and/or an antibody of claim 26, and optionally suitable means for detection.

29. A method for treating of a tumor comprising administering to the subject the pharmaceutical composition of claim 27 in an effective dose.

30. A method for preventing of a tumor comprising administering to the subject the pharmaceutical composition of claim 27 in an effective dose.

31. A method for delaying the reoccurrence of a tumor comprising administering to the subject the pharmaceutical composition of claim 27 in an effective dose.

32. The method of 29, 30 or 31 wherein the tumor is benign or malign and most preferably derived from endocrine or neuronal tissues, i. e. breast, lung, colon, intestine, stomach, prostate, testis, ovary, thyroid, pancreas.

33. A method for treating of neuronal disorders comprising administering to the subject the pharmaceutical composition of claim 27 in an effective dose.

34. A method for preventing neuronal disorders comprising administering to the subject the pharmaceutical composition of claim 27 in an effective dose.

35. A method for delaying the reoccurrence of neuronal disorders comprising administering to the subject the pharmaceutical composition of claim 27 in an effective dose.

36. A method for detecting expression of a tumor suppressor by detecting the presence of mRNA coding for a tumor suppressor which comprises

(a) obtaining mRNA from a cell;

(b) contacting the mRNA so obtained with a probe comprising a nucleic acid molecule of claim 18 under hybridizing conditions; and

(c) detecting the presence of mRNA hybridized to the probe and thereby detecting the expression of the tumor suppressor by the cell.

37. A method for detecting expression of a tumor suppressor by detecting the presence of a tumor suppressor which comprises:

(a) obtaining a cell sample from the subject;

(b) contacting the cell sample so obtained with an antibody of claim 26 under conditions permitting binding of the antibody to the tumor suppressor; and

(c) detecting the presence of the antibody so bound and thereby detecting the expression of the tumor suppressor.

38. The method of claim 37 for the detection of the expression of a tumor suppressor which has lost its tumor suppressor activity.

39. A method for diagnosing in a subject a predisposition to a tumor or to a disorder associated with the expression of a tumor suppressor allele which comprises:

(a) isolating DNA from victims of the tumor or the disorder;

(b) digesting the isolated DNA of step (a) with at least one restriction enzyme;

(c) electrophoretically separating the resulting DNA fragments on a sizing gel;

(d) contacting the resulting gel with a probe comprising a nucleic acid molecule of claim 18 labeled with a detectable marker;

(e) detecting labeled bands on a gel which have hybridized to the probe as defined in (d) to create a band pattern specific to the DNA of victims of the tumor or the disorder;

(f) preparing subject's DNA by steps (a) to (e) to produce detectable labeled bands on a gel; and

(g) comparing the band pattern specific to the DNA of victims of the tumor or the disorder of step (e) and the subject's DNA of step (f) to determine whether the patterns are the same or different and to diagnose thereby predisposition to the tumor or the disorder if the patterns are the same.

40. Use of an effective dose of a nucleic acid molecule of claim 1 or of any one of claims 11 to 17, or a nucleic acid molecule which is complementary to such a nucleic acid molecule for the preparation of a pharmaceutical composition for treating, preventing and/or delaying of reoccurrence of a disease in a subject.

41. Use of an effective dose of a nucleic acid molecule of claim 18 for the preparation of a pharmaceutical composition for treating, preventing and/or delaying of reoccurrence of a disease in a subject.

42. Use of an effective dose of a vector of claim 19 ~~or 20~~ for the preparation of a pharmaceutical composition for treating, preventing and/or delaying of reoccurrence of a disease in a subject.

43. Use of an effective dose of a polypeptide of claim 25 for the preparation of a pharmaceutical composition for treating, preventing and/or delaying of reoccurrence of a disease in a subject.

44. Use of an effective dose of an antibody of claim 26 for the preparation of a pharmaceutical composition for treating, preventing and/or delaying of reoccurrence of a disease in a subject.

45. The use of ~~any one of claims 40 to 44~~ claim 40 wherein the disease is a tumor or a neuronal disorder.

46. The use of claim 45 wherein the tumor is benign or malign and most preferably derived from endocrine or neuronal tissues, i.e. breast, lung, colon, intestine, stomach, prostate, testis, ovary, thyroid, pancreas.

47. A process for identifying compounds effective as antagonists/inhibitors or agonists/activators to a tumor suppressor comprising:

(a) contacting a cell which expresses the polypeptide of claim 25 with a compound to be screened; and

(b) determining if the compound inhibits or enhances activation of the tumor suppressor.

48. An antagonist/inhibitor or agonist/activator to the polypeptide of claim 25 or identified according to the method of claim 47.